REMARKS

Before entry of this Amendment, claims 1, 8, 12-58, and 85-87 were pending. Claims 32-41, 45-58, and 85-87 have been withdrawn from consideration as being drawn to non-elected inventions.

Claims 1, 14-15, and 20 have been amended to improve clarity and more particularly point out certain characteristics of the claimed invention. New claims 93-94 have been added. Support for the claim amendments and new claims can be found in the specification (e.g., the paragraph bridging pages 1 and 2; page 13, lines 24-29; page 67, line 15 – page 68, line 20) and original claims (e.g., claims 12-17). No new matter has been introduced and no new issues have been raised. These amendments have been made solely to expedite allowance of claims. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Claim Rejections under 35 U.S.C. § 102(b)

Claims 1, 8, and 19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Morser et al. (US Patent No. 5,864,018), and as evidenced by Neeper et al. (J. Biol Chem, 1992, 267: 14998-5004), and as newly evidenced by Mjalli et al. (US 2006/0078562). Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Specifically, the Examiner asserts that "[a]lthough the [Morser et al.] patent does not explicitly recite the sequence information for full-length human RAGE, it inherently teaches such, since it teaches the term 'RAGE polypeptide' (see e.g. col.2, lines 45-47; col.8, lines 7-14). Accordingly, this human RAGE polypeptide comprises amino acid residues 1-404 of SEQ ID NO: 7, and this sequence information was well known in the art at the time of filing, as evidenced by Neeper et al. (see p. 15001, Figure 3). Thus, the Morser et al. patent inherently teaches a RAGE polypeptide, which is 100% identical to the instant SEQ ID NO: 7, and therefore meets the limitation of the RAGE-LBE comprising residues 1-344 of SEQ ID NO: 7." Office Action, page 3, lines 16-23.

Applicants respectfully disagree for the reasons already made of record. Nonetheless, solely for greater clarity, Applicants have amended independent claim 1 to recite that "said immunoglobulin element comprises at least one sequence selected from: an immunoglobulin heavy chain, an Fc domain, and a CH1 domain" (e.g., the subject matter of claims 12-17). The Examiner has acknowledged that claims 12-17 are novel over the cited references. These amendments have been made solely to expedite allowance of claims. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants believe that the claim amendments render the rejection moot. Thus, all pending claims are novel over Morser et al. Reconsideration and withdrawal of this rejection are respectfully requested.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 1, 8, 13, and 19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Morser et al. (US Pat. No. 5,864,018), in view of Neeper et al., and further in view of Peppel et al. (J Exp Med. 1991, 174(6):1483-9). Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

The criteria for establishing a *prima facie* case of obviousness are detailed in MPEP §§ 2142-2143. To establish a *prima facie* case of obviousness for combining prior art reference teachings to arrive at the claimed invention, the following three criteria must be met. The prior art references must teach or suggest each and every limitation of the claimed invention. There must be a finding that there was some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Finally, there must be a finding that there was a reasonable expectation of success. Applicants note that the *KSR* decision did not alter these basic requirements for establishing a *prima facie* case of obviousness. As such, the Examiner still has the initial burden of establishing a *prima facie* case of obviousness. In this case, the teachings of Morser et al. in combination with the teachings of Neeper et al. and Peppel et al. fail to satisfy these criteria, and thus fail to undermine the patentability of the claimed invention.

Morser et al. fail to teach or suggest each and every limitation of the claimed invention. As described above, Morser et al. fail to teach or suggest an immunoglobulin element which comprises at least one sequence selected from: an immunoglobulin heavy chain, an Fc domain, and a CH1 domain, as recited in claim 1. In addition, although Morser et al. mention soluble RAGE fragments, Morser et al. do not teach or suggest a RAGE-LBE which consists of amino acid residues 1 through 344 of SEQ ID NO: 7, as recited in claim 1.

Contrary to the Examiner's assertion, the other cited references (Neeper et al. and Peppel et al.) fail to overcome the deficiencies of Morser et al., at least with respect to a RAGE-LBE which consists of amino acid residues 1 through 344 of SEQ ID NO: 7. First, Neeper et al. teach cloning and expression of the full-length RAGE protein. Neeper et al. disclose the sequence and location of the transmembrane domain of human RAGE (e.g., Figure 4). However, Neeper et al. do not teach or suggest a fragment of RAGE such as the RAGE-LBE which consists of amino acid residues 1 through 344 of SEQ ID NO: 7. Second, Peppel et al. describe a chimeric protein comprising a TNF-alpha receptor and a Fc domain. Peppel et al. are entirely silent on the RAGE protein, let alone a fragment of RAGE such as the RAGE-LBE which consists of amino acid residues 1 through 344 of SEQ ID NO: 7. Accordingly, the combined teachings of Morser et al., Neeper et al., and Peppel et al. fail to teach or suggest each and every limitation of the claimed invention.

Even if the Morser reference is to be combined with Neeper et al. and Peppel et al., the combination fails to provide any motivation or reasonable expectation of success for a skilled artisan to modify Morser's RAGE polypeptides to arrive at the RAGE-LBE fusion protein as claimed in claim 1. None of the cited references provide any teaching or suggestion to modify RAGE polypeptides to improve their suitability or efficacy for any application. There is simply no common connection between these cited disclosures that would have motivated a person skilled in the art to combine these teachings to make the RAGE-LBE fusion protein as recited in claim 1. In addition, none of the cited references provide any guidance on how to modify the RAGE protein to arrive at the RAGE-LBE fusion protein as recited in claim 1. As a result, a skilled artisan could not predict that a biologically active RAGE-LBE fusion protein of claim 1 would be successfully made,

no less that it would be useful for treating a disease. In contrast, the present specification describes successful production and therapeutic application of the RAGE-LBE fusion protein of claim 1.

Applicants believe that claim 1 as amended is not obvious over the cited references. For the same reasons, all claims depending from claim 1 (including claims 8, 13, and 19) are not obvious over the cited references. Applicants respectfully request reconsideration and withdrawal of the rejection of the pending claims under 35 USC § 103.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 12, 14-18, 20-31, and 42-44 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Morser et al. (US Pat. No. 5,864,018), in view of Neeper et al. and Peppel et al. as applied to claims 1, 8, 13, and 19 above, and further in view of Milne Edwards et al. and as evidenced by Spriggs et al. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Applicants submit that the combination of the cited references fails to satisfy the criteria necessary for rendering the claimed invention obvious.

As described above, independent claim 1 is not rendered obvious by the combination of Morser et al., Neeper et al., and Peppel et al. The other two cited references (Milne Edwards et al. and Spriggs et al.) do not overcome the deficiencies of those three references. Thus, claim 1 and its dependent claims (including claims 12 and 14-18) are not obvious over the cited references.

Further, Applicants submit that independent claim 20 is not obvious over the cited references. As described above, Morser et al., alone or in combination with Neeper et al. and Peppel et al., do not teach or suggest a RAGE-LBE which consists of amino acid residues 1 through 344 of SEQ ID NO: 7 as recited in claim 20. Further, Morser et al. do not teach or suggest a dimerizing polypeptide, a purification polypeptide, a stabilizing polypeptide, or a targeting polypeptide as recited in claim 20. Thus, Morser et al., alone or in combination with Neeper et al. and Peppel et al., fail to teach or suggest each and every limitation of claim 20.

Milne Edwards et al. disclose production of about 240 different recombinant polypeptides (SEQ ID NOs: 242-482), including fusion proteins which comprise heterologous domains such as

Fc or leucine zippers. However, Milne Edwards et al. do not disclose production of any recombinant RAGE polypeptide, let alone the RAGE-LBE fusion proteins as recited in claim 20. Nor do Milne Edwards et al. teach or suggest an association of the RAGE protein with any disease. Milne Edwards et al. are entirely silent on the RAGE protein. Similarly, Spriggs et al. are entirely silent on the RAGE protein. Spriggs et al. merely describe fusion proteins comprising jun and fos leucine zippers. However, Spriggs et al. do not disclose any recombinant RAGE polypeptide, let alone the RAGE-LBE fusion proteins as recited in claim 20.

Even if Morser et al., Neeper et al., and Peppel et al. are combined with Milne Edwards et al. and Spriggs et al., the combination still fails to provide any suggestion or motivation for a skilled artisan to modify Morser's RAGE polypeptides to arrive at the claimed RAGE-LBE fusion protein as recited in claim 20. None of the cited references provide any teaching or suggestion to modify RAGE polypeptides to improve their suitability or efficacy for any application. There is simply no common connection between these cited disclosures that would have motivated a person skilled in the art to combine these teachings to make the RAGE-LBE fusion protein as recited in claim 20. In addition, none of the cited references provide any guidance on how to modify the RAGE protein to arrive at the RAGE-LBE fusion protein as recited in claim 20. As a result, a skilled artisan could not predict that a biologically active RAGE-LBE fusion protein of claim 20 would be successfully made, no less that it would be useful for treating a disease. In contrast, the present specification describes successful production and therapeutic application of the RAGE-LBE fusion protein of claim 20.

Applicants submit that claim 20 is not obvious over the cited references. For the same reasons, all claims depending from claim 20 are not obvious over the cited references. Applicants respectfully request reconsideration and withdrawal of the rejection of the pending claims under 35 USC § 103.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (617) 951-7000. Applicants believe that no fee is due. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. **PCFC-243-101** from which the undersigned is authorized to draw.

Dated: May 19, 2010

Respectfully submitted,

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